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REAL-WORLD CLINICAL OUTCOMES TWO YEARS AFTER TRANSITION TO PSYCHOSIS IN INDIVIDUALS AT CLINICAL HIGH RISK: ELECTRONIC HEALTH RECORD COHORT STUDY

Paolo Fusar-Poli[1,2,3,4], Andrea De Micheli[1,2], Rashmi Patel[5], Lorenzo Signorini[1], Syed Miah[1], Thomas Spencer[2,5], Philip McGuire[2,4,5]

Affiliations

[1] Early Psychosis: Interventions and Clinical-detection (EPIC) lab, Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK;

[2] OASIS service, South London and Maudsley NHS Foundation Trust, London, UK;

[3] Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy;

[4] National Institute for Health Research, Maudsley Biomedical Research Centre, South London and Maudsley NHS Foundation Trust, London, UK;

[5] Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK;

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Correspondence to: Dr Paolo Fusar-Poli MD PhD, Department of Psychosis Studies, 5th Floor, Institute of Psychiatry, Psychology & Neuroscience, PO63, 16 De Crespigny Park, SE5 8AF London, UK. E-mail: paolo.fusar-poli@kcl.ac.uk

ABSTRACT

Objective

To describe the two-year real-world clinical outcomes after transition to psychosis in patients at clinical high-risk.

Methods

Clinical Electronic Health Record (EHR) cohort study including all patients receiving a first index primary diagnosis of non-organic ICD-10 psychotic disorder within the early psychosis pathway in the SLaM NHS Trust from 2001 to 2017. Outcomes encompassed: cumulative probability (by 3-, 6-, 12-, 24-months) of receiving a first (i) treatment with antipsychotic, (ii) informal admission and (iii) compulsory admission, (iv) treatment with clozapine and (v) numbers of days spent in hospital (by 12- and 24-months) in patients transitioning to psychosis from clinical high-risk services (OASIS) compared to other first-episode groups. Analyses included logistic and zero-inflated negative binomial regressions.

Results

1,561 patients were included; those who had initially been managed by OASIS and had subsequently transitioned to a first-episode of psychosis (n=130) were more likely to receive antipsychotic medication (by 3-, 6-, 24-month, all $P<0.023$), to be admitted informally (at all timepoints, all $P<0.004$) and on a compulsory basis (at all timepoints, all $P<0.013$), and to have spent more time in hospital (all timepoints, all $P<0.007$) than first-episode patients who were already psychotic when seen by the OASIS service (n=310), or presented to early intervention services (n=1,121). The likelihood of receiving clozapine was similar across all groups (by 12-/24-month, all $P<0.101$).

Conclusions

Transition to psychosis from a clinical high-risk state is associated with severe real-world clinical outcomes. Prevention of transition to psychosis should remain a core target of future research.

Study protocol registration: researchregistry5039 (www.researchregistry.com).

INTRODUCTION

Preventive approaches in young, help-seeking individuals presenting with attenuated psychotic symptoms[1] and functional impairments[2] to specialised clinical services, and meeting a Clinical High-Risk state for Psychosis (CHR-P)[3], have the potential to maximise the benefits of early interventions for the most severe psychiatric disorder[4,5]. Two decades since being first conceived[6,7], the essence of the CHR-P paradigm remains its capacity to prospectively identify individuals at increased risk of "transition" to psychosis from an at-risk stage[8]. Accordingly, research has mostly focused on the identification of robust predictors of transition to psychosis[9] or on effective treatments to prevent a first-episode of psychosis (FEP)[10] from a CHR-P state.

However, the concept of transition to psychosis from a CHR-P state has always been under fire. Transition to psychosis is dichotomously defined (i.e. transition to psychosis vs non-transition to psychosis) in terms of "above-threshold" (i.e. more than a certain cutoff of severity and/or frequency on the CHR-P psychometric instruments[11]) positive psychotic phenomena, such as delusions and hallucinations[8]. Such a threshold is psychometrically arbitrary because it was introduced to guide the clinical commencement of antipsychotic treatments in CHR-P individuals[12]. Furthermore, the psychosis threshold in the CHR-P assessment tools is different from that employed in standard ICD and DSM psychiatric classifications[13]. For example, individuals with Brief and Limited Intermittent Psychotic Symptoms are considered at-risk and not psychotic under the CHR-P approach but already psychotic under the ICD or DSM approaches[14,15]. A further bias is that transition to psychosis (as an outcome) is measured on the same dimensional scale that defines the CHR-P state (as a predictor), producing "artificial diagnostic shifts"[16]. Furthermore, the use of a crude dichotomous diagnostic outcome in individuals who frequently have several comorbid non-psychotic mental disorders[17] may be questionable[13], because it does not reflect the underlying clinical complexity. A collateral issue is that the risk of transition to psychosis in CHR-P individuals has declined from 31.5% at 3-year (2012 meta-analysis[18]) to 22% at 3-year (2016 meta-analysis[19]), although not globally[20]. In light of the sampling biases that reduce the epidemiological validity of the paradigm [21], low impact of the CHR-P approach for detecting patients at risk[22,23], and high insight in CHR-P individuals (which is associated with good outcomes[24]), it has been claimed that CHR-P individuals reflect an intrinsically good-prognostic subgroup which represents a "different illness" compared to more sever psychotic disorders such as schizophrenia[16]. There is thus converging criticism across different authors[8,12,13,16] that the concept of transition to psychosis from a CHR-P stage may be irrelevant in terms of real-world clinical outcomes[16]. Over the past decade, several authors have indicated that it is essential to test whether the transition to psychosis in CHR-P

individuals has any validity in terms of outcome[12] but surprisingly no large-scale studies have been published to date.

This study addresses this gap in knowledge by describing, for the first time, the real-world clinical outcomes of CHR-P individuals who have transitioned to psychosis, compared to patients who first present at the FEP stage. In line with the evidence above, we hypothesised that CHR-P individuals transitioning to psychosis would represent a subgroup of FEP patients which display better clinical outcomes than other FEP patients.

METHODS

Design

Retrospective cohort study using Electronic Health Records (EHRs).

Data source

The Clinical Record Interactive Search -CRIS- tool (CRIS[25]) provides contemporaneous EHR and 'real-world' data on routine mental healthcare[26] from all patients managed by the South London and Maudsley (SLaM) NHS Foundation Trust. SLaM is a UK National Health Service (NHS) mental health trust that provides secondary mental health care to a population of 1.36 million individuals in South London (Lambeth, Southwark, Lewisham and Croydon boroughs). In SLaM there is one of the highest rates of psychosis in the world[27]. In terms of the quality of SLaM/CRIS records, SLaM was an early pioneer of electronic health records and the trust is effectively digitised and paper-free[25]. SLaM has a near-monopoly in terms of secondary mental healthcare provision to its local catchment area, and it is a legal requirement for SLaM healthcare professionals to keep these records up to date[25]. Whereas many national registers capture only those patients who have been hospitalised, the SLaM/CRIS register contains the full clinical records of all patients, which are continually updated throughout their care, regardless of discharges from and/or referrals to other services.

Study population

All individuals accessing SLaM from January 2001 to July 2017 and receiving a first primary diagnosis of non-organic ICD-10 psychotic disorder (see eMethod 1) in the local early psychosis pathway. SLaM covers a catchment area in South-London encompassing the boroughs of Lambeth (total population, 334,724) and Southwark (total population, 322,302), Lewisham (total population, 310,324) and Croydon (total population, 391,296) [28]. Incidence of psychosis in Lambeth, Southwark, Lewisham and Croydon is estimated at 71.9, 69.6, 71.3, 58.3 cases per 100,000 person-years respectively, which is higher than England

national average of 34.9 cases[28]. In SLaM there is one of the highest incidence of psychosis of the world[29].

The local early psychosis pathway included: Early Intervention Services (EI) for assessment and treatment of individuals with FEP, and early detection services such as the Outreach And Support In South-London (OASIS[30]) for individuals with CHR-P. However, about one third of referrals to OASIS are presenting with FEP[31] and are immediately referred to EI for treatment (see below). Individuals who were given a first primary diagnosis of non-organic ICD-10 psychotic disorder by either EI or OASIS services were initially included. Subsequently, individuals who did not match the age range of the OASIS-T group (below) were subsequently excluded. The individuals thus selected were then assigned to three non-overlapping clinical subgroups that are described below.

Clinical subgroups

OASIS[30] is an early detection service which was set up in 2001, and it is one of the oldest CHR-P services in the UK[30]. OASIS focuses on the identification, prognostic assessment and treatment of help-seeking CHR-P individuals aged 14-35 years, serving the same catchment area population as other SLaM services (below). OASIS is integrated in the Pan-London Network for Psychosis-prevention (PNP)[28]. The OASIS-transitioning (OASIS-T) group comprised patients who had initially presented to OASIS with a CHR-P state (ascertained using the Comprehensive Assessment of At Risk Mental States, CAARMS[32]), and who had subsequently transitioned to psychosis during a 2-year follow-up period.

OASIS receives referrals from a variety of agencies[30], and about one-third of them represents undetected cases of FEP from the community (OASIS-First Episode, OASIS-FEP)[31]. This group included individuals who had been referred to OASIS but on initial CAARMS assessment were found to already be experiencing a FEP (rather than CHR-P). In both the OASIS-T and OASIS-FEP groups, the diagnostic threshold for a FEP was assessed by OASIS clinicians using the CAARMS.

The Early Intervention-First Episode (EI-FEP) group included patients who received a diagnosis of FEP from SLaM EI services, and not from the OASIS as it is the case of the OASIS-FEP group. These services (established in 2001[33,34]) closely interact with OASIS and are specialised for patients with FEP, comprising an assertive outreach community team in each of the four SLaM boroughs, as well as an inpatient unit. These services provided care for individuals aged 16-35 until April 2016, after which the upper age limit was extended to 65[35].

Because all OASIS patients upon transition (OASIS-T) or detection (OASIS-FEP) are typically referred to EI services, the current cohort has been offered the same standard type of care for FEP throughout the course of the study. The type of FEP care is mandated by the NICE Clinical Guideline 178 (https://www.nice.org.uk/guidance/cg178)[36] which have been implemented in 2014 and became a national standard. This included crisis resolution and home treatment teams, which became mandatory in England in 2000 under the National Health Service (NHS) Plan[37] and operate around the clock, offering rapid access and intensive support in the community to prevent the need of hospitalisation[38,39]. The first-line recommended therapy of EI services following FEP onset is antipsychotic medication alongside psychosocial interventions[36].

Approval for the study was granted by the Oxfordshire Research Ethics Committee C. Because the dataset comprised de-identified data, informed consent was not required[25].

Study measures

Variables

Baseline descriptive variables included sociodemographic (age, sex, ethnicity, marital status, employment status, accommodation status) and clinical characteristics (the diagnostic cluster and Health Of the Nation Outcome Scale [HONOS][40], eMethod 1). Additional baseline variables that described the OASIS-T patients ahead of their development of psychosis onset included the type of CHR-P, classified as APS (APS only or APS plus GRD), BLIPS (BLIPS only, BLIPS plus APS or BLIPS plus APS plus GRD) and GRD only, in line with previous studies[41], the severity of CHR-P symptoms (operationalised as the summed scores of the product of global rating scale score (0-6) and frequency (0-6) of the four CAARMS[42] subscales, in line with previous studies[43]) at the time of their first contact with OASIS, functional status (Social and Occupational Functioning Assessment Scale [SOFAS][44]) at first presentation with OASIS and the duration of the CHR-P stage (defined by the period between the first presentation to OASIS and the date of transition to psychosis).

Follow-up

In all groups, follow-up started at the time of their index diagnosis of psychosis and ended when a primary outcome was recorded, or when the patient dropped out of the EHR (as documented by the last entry on CRIS), or when the 2-year follow-up had been completed.

Primary outcomes

The primary outcomes of the current study were the cumulative probability (from intake to 3, 6, 12, 24 months) of first receiving (i) treatment with antipsychotic medication, (ii) informal admission to a mental health hospital, (iii) compulsory admission to a mental health hospital (involving a Mental Health Act -MHA- assessment), (iv) treatment with clozapine, and (v) the numbers of days spent in hospital (by 12 and 24 months) in the OASIS-T group, compared to other FEP groups.

Statistical analysis

This clinical register-based cohort study (study protocol registered on www.researchregistry.com, researchregistry5039) was conducted according to the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement[45] (see supplementary checklist). Sociodemographic and clinical characteristics of the sample (including missing data), were described with mean and SD for continuous variables, absolute and relative frequencies for categorical variables, and compared with ANOVA and chi-square tests; post-hoc analyses were conducted to clarify between-groups differences. The cumulative probability of receiving a first treatment with antipsychotic medication, a first informal admission to a mental health hospital, a first compulsory admission to a mental health hospital, and a first treatment with clozapine were investigated with complete-case logistic regression (Odds Ratio, OR) analyses at different timepoints; the number of cases at risk (not dropped out) was reported. Because the numbers of days spent in hospitals were characterised by an excess of zero values and overdispersion, they were analysed with complete-case zero-inflated negative binomial regression analyses, which are suited for modelling count variables with excessive zeros and overdispersed count outcome variables[46]. Furthermore, sensitivity analyses were conducted to test the potential impact of a priori confounders such as the different types of index diagnoses of psychosis[5]. For all analyses, statistical tests were two-sided, and significance was defined as a p-value of < 0.05. All analyses were conducted in STATA 14 (STATA Corp., TX, USA).

RESULTS

Baseline characteristics of the sample

As shown in Figure 1, 1,587 individuals received a primary index diagnosis of ICD-10 non-organic psychotic disorder in SLaM early intervention psychosis pathway services during the study period. The age range of OASIS-T patients at the point of transition to psychosis was 14-38. Therefore, individuals outside this age range (n=26) were excluded from further analysis, leaving a final population of 1,561 individuals (the proportion with missing

diagnostic data was very small). The final cohort included n=130 individuals in the OASIS-T group, n=310 in the OASIS-FEP group and n=1,121 in the EI-FEP. There were no group difference in sex, ethnicity, marital status but significant group differences (Table 1) in age (OASIS-FEP patients were relatively younger than the EI-FEP: F=26.796, P<0.001 and OASIS-T: F=26.253, P=0.003 but there were no differences between the OASIS-T and EI-FEP groups: F=1.68, P=0.195), employment status (there were more students and fewer unemployed patients in the OASIS-T compared to the EI-FEP group: F=30.785, P<0.001 but no differences between the OASIS-T and the OASIS-FEP group: F=4.726, P=0.094), accommodation status (there were more homeless/patients receiving a supported accommodation in the OASIS-T compared to the other groups) HONOS scores (higher in the OASIS-FEP than in the EI-FEP group: F=14.13, P<0.001; no differences between the OASIS-T and the other groups: all P>0.05) and type of index psychotic diagnoses (schizophrenia spectrum psychoses were more frequent in the EI-FEP group, affective spectrum psychoses in the OASIS-T group, psychoactive substance use psychoses in the OASIS-FEP group, Acute and Transient Psychotic Disorders in the EI-FEP group: all F>16.623, all P<0.002). For 6 patients the CHR-P subgroup was not known; among the others there were 87 (70.16%) APS, 36 (29.03%) BLIPS and 1 GRD (0.81%). At the time of presentation to OASIS, the average total CAARMS score was 42.71 (SD=19.22), the average SOFAS was 53.97 (SD 13.19), and the average duration of the CHR-P stage was of 552.27 days (SD 762.55).

Clinical outcomes in CHR-P patients

Cumulative probability of receiving a first treatment with antipsychotic medication

The OASIS-T group was more likely to have received antipsychotic medication than the other three groups by 3-, 6- and 24-month; by 12-month it was more likely to have received antipsychotics than the EI-FEP group, but not the OASIS-FEP group, (Figure 1 and Table 2a; the frequency of antipsychotic treatment by 24-month was: 96.33% OASIS-T, 88.43% OASIS-FEP, 80.29% EI-FEP).

Cumulative probability of receiving a first informal admission to a mental health hospital

The OASIS-T group was more likely to have had an informal admission to a mental health hospital than the other two groups at all timepoints (Figure 1, Table 2a and 2b; the frequency of informal admission by 24-month was: 47.56% OASIS-T, 29.27% OASIS-FEP, 18.20% EI-FEP).

Cumulative probability of receiving a first compulsory admission to a mental health hospital

The OASIS-T group was more likely to have had a compulsory admission to a mental health hospital than the other two groups at all timepoints (Figure 1, Table 2a and 2b; the frequency of compulsory admission by 24-month was: 46.51% OASIS-T, 29.35% OASIS-FEP, 20.96% EI-FEP).

Cumulative probability of receiving a first treatment with clozapine

There were no patients receiving clozapine by 3- and 6-month. However, by 12- and 24-month, there was no significant difference in the likelihood of having been treated with clozapine between the OASIS-T patients and the other two groups (Table 2a and 2b; by 24 months clozapine frequency was 6.94% in OASIS-T, 3.16% in OASIS-FEP, 3.21% in EI-FEP). Since these results are based on small counts, they are not plotted in Figure 1.

Numbers of days spent in hospital

The OASIS-T patients spent more days in mental health hospitals than any other group by both 12- (any $P<0.001$) and 24-month (any $P<0.007$; by 24-month: OASIS-T 63.21 days, SD=128.44; OASIS-FEP 29.14 days, SD 72.33; EI-FEP 1.86 days, SD 17.95).

Sensitivity analyses

The type of ICD10 index psychotic diagnoses did not impact any outcome, with the exception of the days spent in hospitals: the OASIS-T group spent more days in mental health hospitals than the EI-FEP and FEP -but not OASIS-FEP- groups by 12-month (eResults 2a and 2b).

DISCUSSION

To our knowledge, this is the first large-scale cohort study to examine clinical outcomes in CHR-P individuals transitioning to psychosis compared to other patient groups receiving an index diagnosis of a FEP. This group had more severe clinical outcomes than FEP patients whose first presentation to services was when they were frankly psychotic.

Because only a minority of CHR-P individuals develop psychosis (22% by 3-year[19]), it is challenging to ascertain large samples that have transitioned to psychosis. A strength of the present study is that the largest cohort of CHR-P subjects which was followed clinically for two years after they had become psychotic (n=130). Further strengths were that the OASIS-T group was compared with age-matched FEP groups, and the psychosis threshold and index diagnoses were measured using an anchor (i.e. the ICD) independent to that used to define the CHR-P state (i.e the CAARMS). Clinical follow-up of large numbers of patients was facilitated by the use of well-validated software for searching EHRs[26,47].

Contrary to our hypothesis, the OASIS-T group had significantly more severe clinical outcomes than the other two FEP groups on most measures, at most timepoints: they were more likely to have received antipsychotic treatment (by 3-, 6-, 24-month), to have been admitted informally (at all timepoints) and on a compulsory basis (at all timepoints) to mental health hospital, and spent more days in hospital (at all timepoints). In the context of a naturalistic and non-randomised study, these results should be interpreted with caution. Associations (i.e. ORs) are not causations, and potential clinical and sociodemographic confounders must be considered.

The main between-group differences related to the type of psychotic disorders. Since the type of psychotic disorder (e.g. schizophrenia spectrum vs other types of psychotic disorders), is associated with clinical outcomes[5], we entered this covariate in the analyses. The core results remained unchanged. The OASIS-T group included a similar proportion of black and female people and had a comparable average age and HONOS score than the EI-FEP group. Despite the higher proportion of students, the OASIS-T also included higher proportions of socially deprived (e.g. homeless) people, and the average HONOS score (an index of overall clinical severity) was 12.84, compared to 8.05 for patients discharged from inpatient mental health units[48]: social deprivation and higher baseline clinical severity have previously been associated with more severe outcomes in patients with psychosis[49,50]. Therefore, these findings contradict the assumptions that because this population is help-seeking, it is higher functioning, better educated, more affluent and more likely to be white than a typical patient with psychosis. Contrary to previous claims[16], we found no evidence that patients who develop psychosis after first being seen by CHR-P services represent a subgroup with relatively good outcomes.

Other potential confounders could be treatments received over follow-up and pathways to care. However, we found that they had more severe clinical outcomes at almost all of the follow-up timepoints, despite having received clinical care during the CHR-P phase (needs-based interventions encompassing close-in monitoring, psychosocial support and psychoeducation[51]) and cognitive behavioural therapy (whose specific efficacy is uncertain[10,52,53]) that was not provided to the other FEP patients. Furthermore, on transition to psychosis, OASIS-T patients were typically referred to the local EI services; therefore, all patients in the current study were offered the standard type of care recommended for FEP, which aligns with the NICE clinical guidance 178. It is thus unlikely that systematic differences in the local package of care received may have confounded the outcomes observed.

Our current findings confirm recent studies which suggest that a history of symptoms consistent with a CHR-P state (in this case assessed by retrospectively screening health records in FEP patients in the absence of a real CHR-P interview and prospective follow-up for transition) is associated with more severe psychotic symptoms and poorer global functioning 1 year following a FEP[54]. The present study extends these findings by demonstrating that outcomes are also more severe 2 years after psychosis onset, even in patients who received a high level of specialised mental health input that is designed to prevent transition to psychosis during the CHR-P phase. This raises the possibility that these patients may actually have a more insidious and severe form of psychotic disorder than other FEP patients.

Further evidence that CHR-P patients who transition to psychosis do not represent a good prognosis subgroup was available from rates of clozapine prescribing after illness onset. By both 12- and 24-months OASIS-T patients were just as likely (6.94%) as the other groups (e.g. EI-FEP 3.21%) to have received clozapine treatment, which is a proxy marker for treatment-resistant psychosis. Although this finding is based on limited statistical power and therefore it should be interpreted cautiously, it is in line with a previous small-scale report showing that CHR-P patients (n=18) who transitioned to psychosis were more likely to have been prescribed more than one antipsychotic medication (90% vs 68%) and to have received clozapine (38% vs 2%) than FEP patients detected by EI services[55].

Overall, the current study confirms that developing a FEP following a CHR-P stage has a prognostic value for predicting clinical outcomes[54]. The findings of the current study considered together indicate that transition to psychosis after a CHR-P stage is not a “trivial” event[16] because it is associated with more severe real-world outcomes compared to other patients with FEP. While future research is certainly needed to better address the heterogeneous clinical outcomes of this population, such as remission or persistence of disability or functional impairment[56], this should not happen at the expense of dismissing transition to psychosis. The main clinical implication is that drug development and discovery should still consider prevention of psychosis onset from a CHR-P stage as an important clinical outcome. On a parallel line, our findings can also inform clinical guidelines to clearly recommend close monitoring and intensive care for CHR-P individuals who transition to psychosis.

One limitation of this study is that it did not employ structured psychometric interviews to ascertain the index psychotic diagnoses and their diagnostic stability[57]. Therefore, while the current EHR findings have high ecological validity (i.e. they represent real-world clinical

practice), they have not been subjected to formal validation with research-based criteria. However, while this issue is relevant for patients who presented to generic mental health services, in those that were assessed by OASIS or EI teams the diagnosis of FEP was formulated by experienced clinicians with specialist expertise in the assessment and diagnosis of emerging psychosis. Furthermore, the aim of the present study was to assess real-world clinical outcomes rather than psychometric outcomes in FEP; the use of structured diagnostic interviews in research settings can itself lead to the selection of white, more highly educated and "squeaky-clean"[58] patient subsamples[59], further exaggerating sampling biases that are already affecting this field[21]. There is also meta-analytical evidence indicating that for psychotic categories, administrative data recorded in clinical registers are generally predictive of a true diagnosis[60] (see also eLimitation). Another limitation is that patients moving outside the SLaM catchment area may have not been followed up. However, with the exclusion of clozapine treatment, for any other outcome the proportion of missing data at follow up was less than 4%. A further limitation is that, because of HONOS data missingness at follow-up, we were unable to use HONOS changes from baseline to follow-up as a covariate. Importantly, the current study simply described outcomes without addressing the effectiveness of early detection (CHR-P) clinics compared to other mental health services. Testing the effectiveness of CHR-P clinics would require randomised designs, which are ethically and logistically difficult to implement. Because of these limitations, it is not possible to interpret the results of the current study to conclude that CHR-P services are ineffective in improving outcomes of these patients. It is still possible that individuals who access CHR-P clinics and who would later on develop psychosis would have a chance of having prevented such transition, while those who do convert may be the ones with an inherently insidious outcome and poor prognosis.

CONCLUSION

Transition to psychosis from a CHR-P state is associated with more severe real-world clinical outcomes than in other FEP patients. There was no evidence to support the notion that CHR-P individuals who transition to psychosis represent an atypical good prognosis subgroup. While future replication studies are needed, these findings indicate that prevention of psychosis in CHR-P individuals should remain a core target of empirical prognostic and interventional research.

DETAILS OF CONTRIBUTORS

PFP conceived and led the study. ADM, RP, LS, SM, TS gave substantial contributions to the acquisition and interpretation of data. PFP drafted the work and conducted the analyses. PM gave substantial contributions to the interpretation of the results.

PFP, ADM, RP, LS, SM, TS, PM revised it critically for important intellectual content. All authors approved the final version to be published and agreed to be accountable for all the aspects of the work. PFP had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

NON-AUTHOR CONTRIBUTIONS

None

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DATA SHARING STATEMENT

There is no ethical approval for data sharing.

Figure 1. Flow chart of the study population. OASIS-T: FEP patients detected by OASIS following a clinical high-risk state; OASIS-FEP: FEP patients detected by OASIS at presentation; EI-FEP: FEP patients detected by Early Intervention for psychosis services.

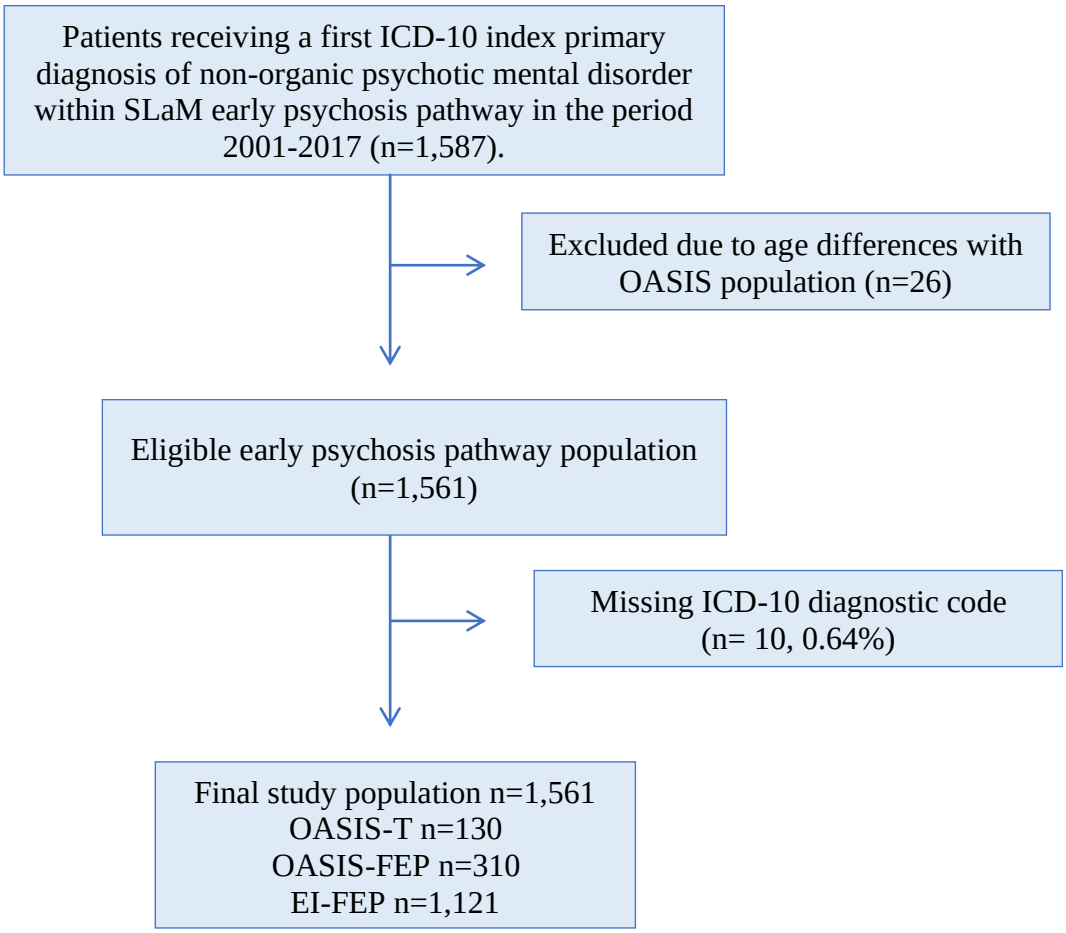

Table 1. Sociodemographic and clinical characteristics of the sample. OASIS-T: FEP patients detected by OASIS following a clinical high-risk state; OASIS-FEP: FEP patients detected by OASIS at presentation; EI-FEP: FEP patients detected by Early Intervention for psychosis services.

		OASIS-T			**OASIS-FEP**			**EI-FEP**				*Test*	
Continuous variables		*N*	*mean*	*SD*	*N*	*mean*	*SD*	*N*	*mean*	*SD*	*SD*	*F*	*P*
Age		130	24.99	5.485	310	23.38	4.896	1121	25.615	5.150	6.428	23.02	<0.001
HONOS tot		80	12.84	6.221	210	13.65	5.539	1040	10.964	10.076	9.837	8.20	0.001
Categorical variables	*Levels*	*N*	*count*	*%*	*N*	*count*	*%*	*N*	*count*	*%*	*%*	*X2*	*P*
Sex		130			310			1121					
	Male		78	60.00		205	66.13		738	65.83	64.11	1.842	0.398
	Female		52	40.00		105	33.87		383	34.17	35.89		
Self-assigned ethnicity		130			306			1075					
	Any white		44	33.85		98	32.03		336	31.26	39.22	3.949	0.683
	Any black		65	50.00		152	49.67		526	48.93	41.97		
	Any Asian		10	7.69		15	4.90		67	6.23	7.75		
	Any other (a)		11	8.46		41	13.40		146	13.58	11.06		
Marital status (b)		121			295			1047				7.640	0.106
	In a relationship		14	11.57		37	12.54		85	8.12	11.37		
	Separated or divorced		5	4.13		7	2.37		42	4.01	4.91		
	Single		102	84.30		251	85.08		920	87.87	83.72		
Employment status (b)		123			290			347				41.127	<0.001
	Employed		27	21.95		68	23.45		44	12.68	8.75		
	Student		38	30.89		61	21.03		46	13.26	9.82		
	Unemployed		58	47.15		161	55.52		257	74.06	81.43		
Accommodation status (b)		118			288			647				12.269	0.015
	Owner		3	2.54		2	0.69		5	0.77	1.33		
	Homeless or supported		30	25.42		42	14.58		139	21.48	17.37		
	Other		85	72.03		244	84.72		503	77.74	81.3		
ICD-10 index diagnosis		126			304			1121				170.95	<0.001
	Schizophrenia spectrum psychoses		26	20.63		53	17.43		257	22.93	49.33		
	Affective spectrum psychoses		29	23.02		34	11.18		71	6.33	10.67		
	Psychoactive substance use psychoses		13	10.32		47	15.46		22	1.96	5.41		
	ATPD		9	7.14		51	16.78		353	31.49	17.03		
	Other psychoses		49	38.89		119	39.14		418	37.29	17.55		

(a) Including mixed ethnicities; (b) self-assigned.

Figure 2. Real-world clinical outcomes in patients with a first-episode of psychotic (FEP) disorder. OASIS-T: FEP patients detected by OASIS following a clinical high-risk state; OASIS-FEP: FEP patients detected by OASIS at presentation; EI-FEP: FEP patients detected by Early Intervention for psychosis services.

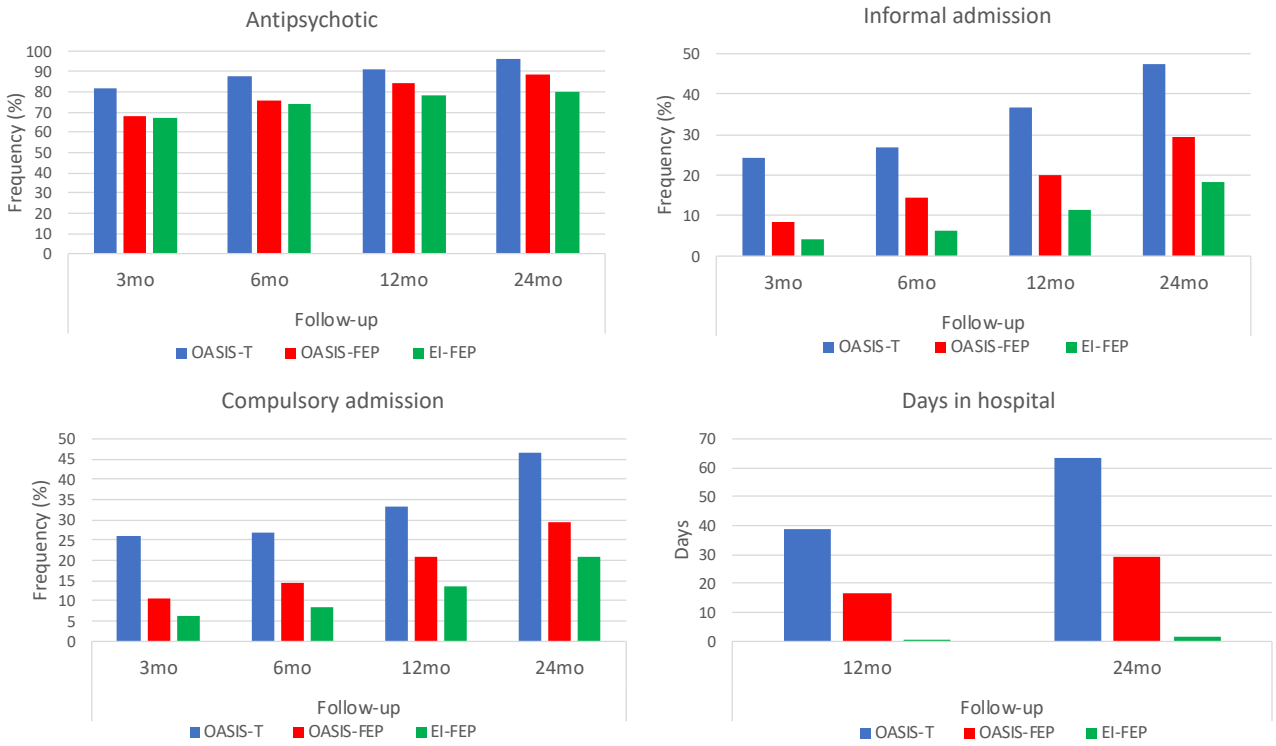

Table 2a. Group differences in real-world clinical outcomes in patients with an index diagnosis of non-organic first-episode of psychosis.

		3 months						6 months					
		N	*OR*	*SE*	*z*	*P*	*95%CIs*	*N*	*OR*	*SE*	*z*	*P*	*95%CIs*
Antipsychotic		1533				0.003		1525				0.001	
	OASIS-T		1						1				
	OASIS FEP		0.475	0.129	-2.74	0.006	0.279 0.809		0.436	0.138	-2.62	0.009	0.234 0.810
	EI-FEP		0.456	0.114	-3.15	0.002	0.280 0.743		0.381	0.112	-3.30	0.001	0.214 0.676
Informal admission		1526				<0.001		1505				<0.001	
	OASIS-T		1						1				
	OASIS FEP		0.298	0.090	-4.02	<0.001	0.165 0.537		0.450	0.124	-2.90	0.004	0.263 0.771
	EI-FEP		0.141	0.037	-7.48	<0.001	0.084 0.235		0.185	0.046	-6.85	<0.001	0.114 0.300
Compulsory admission		1525				<0.001		1502				<0.001	
	OASIS-T		1						1				
	OASIS FEP		0.340	0.097	-3.78	<0.001	0.195 0.595		0.396	0.108	-3.40	0.001	0.232 0.675
	EI-FEP		0.189	0.046	-6.79	<0.001	0.117 0.305		0.215	0.051	-6.49	<0.001	0.135 0.342
Clozapine		1121				(a)		1121				(a)	
	OASIS-T		1(a)						1(a)				
	OASIS FEP		1(a)						1(a)				
	EI-FEP		1						1				
								N	*Coeff*	*SE*	*z*	*P*	*95%CIs*
Days spent in hospital								1477				<0.001	
	OASIS-T								0				
	OASIS FEP								-0.833	0.221	-3.77	<0.001	-1.267 -0.400
	EI-FEP								-4.180	0.358	-11.67	<0.001	-4.882 -3.478

a) There were no cases in this group; OASIS-T: first-episode of psychosis patients detected by OASIS following a clinical high-risk state; OASIS-FEP: first-episode of psychosis patients detected by OASIS at presentation; EI-FEP: first-episode of psychosis patients detected by early intervention for psychosis services.

Table 2b. Group differences in real-world clinical outcomes in patients with an index diagnosis of non-organic first-episode of psychosis

		12 months						24 months					
		N	*OR*	*SE*	*z*	*P*	*95%CIs*	*N*	*OR*	*SE*	*z*	*P*	95%CIs
Antipsychotic		1512				<0.001		1498				<0.001	
	OASIS-T		1						1				
	OASIS FEP		0.516	0.191	-1.79	0.074	0.250 1.066		0.291	0.158	-2.27	0.023	0.100 0.846
	EI-FEP		0.342	0.116	-3.17	0.002	0.176 0.664		0.155	0.080	-3.62	<0.001	0.057 0.426
Informal admission		1465				<0.001		1408				<0.001	
	OASIS-T		1						1				
	OASIS FEP		0.437	0.114	-3.17	0.002	0.262 0.729		0.456	0.123	-2.92	0.004	0.269 0.773
	EI-FEP		0.219	0.050	-6.69	<0.001	0.140 0.342		0.245	0.057	-6.00	<0.001	0.155 0.388
Compulsory admission		1465				<0.001		1408				<0.001	
	OASIS-T		1						1				
	OASIS FEP		0.521	0.137	-2.48	0.013	0.311 0.873		0.478	0.127	-2.78	0.005	0.284 0.805
	EI-FEP		0.319	0.072	-5.03	<0.001	0.204 0.497		0.305	0.070	-5.20	<0.001	0.195 0.477
Clozapine		1455				0.213		1383				0.318	
	OASIS-T		1						1				
	OASIS FEP		0.198	0.244	-1.31	0.189	0.018 2.213		0.437	0.272	-1.33	0.183	0.129 1.479
	EI-FEP		0.810	0.609	-0.28	0.779	0.186 3.532		0.445	0.219	-1.64	0.101	0.169 1.170
								N	*Coeff*	*SE*	*z*	*P*	*95%CIs*
Days spent in hospital								1403				<0.001	
	OASIS-T								0				
	OASIS FEP								-0.774	0.287	-2.7	0.007	-1.337 -0.212
	EI-FEP								-3.525	0.356	-9.89	<0.001	-4.224 -2.827

OASIS-T: first-episode of psychosis patients detected by OASIS following a clinical high-risk state; OASIS-FEP: first-episode of psychosis patients detected by OASIS at presentation; EI-FEP: first-episode of psychosis patients detected by early intervention for psychosis services.

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